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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/654,276	09/01/2000	Smadar Cohen	9124.117US01	5848

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EXAMINER	
WEHBE, ANNE MARIE SABRINA	
ART UNIT	**PAPER NUMBER**
1633	

DATE MAILED: 06/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/654,276	COHEN ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5,6,9,10 and 16-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-3,5,6,9,10 and 22* is/are allowed.

6)☒ Claim(s) *16-21, and 23-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and response received on 4/8/05 has been entered. Claims 1-3, 5-6, 9-10, and 16-24 are currently pending and under examination in the instant application. An action on the merits follows.

Those sections of Title 35, US code, not included in the instant action can be found in the previous office action.

Claim Rejections - 35 USC § 103

The rejection of claims 1-3, 5-6, 9-10, and 16-24 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,099,832 (8/8/00), hereafter referred to as Mickle et al., in view of WO 97/44070 (11/27/97), hereafter referred to as Shapiro et al., is **maintained** over claims 16-21, 23, and 24, and **withdrawn** over claims 1-3, 5-6, 9-10, and 22.

The rejection has been withdrawn over claims 1-3, 5-6, 9-10, and 22 in view of applicant's arguments based on Li et al. reference, provided with the instant response. Li et al. was published before the effective filing date of the instant application by the same group that authored the primary reference in this rejection, Mickle et al. The Li et al. publication states that transplantation of a bioengineered cardiac graft comprising a biodegradable gelatin inoculated *ex vivo* with cardiomyocytes such that a three dimensional beating cardiac graft was formed did not demonstrate any therapeutic effect on cardiac function. In view of this evidence, applicant's

argument that Mickle et al. does not provide a reasonable expectation of success in repairing damaged myocardium using a therapeutic graft comprising a biodegradable scaffold supporting cells comprising a combination of adult or pediatric cardiomyocytes and endothelial cells is found persuasive.

Applicant's arguments as they pertain to the subject matter in claims 16-21, and 23-24 have been fully considered but have not been found persuasive in overcoming the instant grounds of rejection for reasons of record as discussed in detail below.

The applicant argues that the rejection of record does not meet one or more of the criteria for establishing a *prima facie* case of obviousness. First, the applicant argues that Mickle et al. does not teach that a polysaccharide scaffold seeded with cells. The applicant states that Mickle only exemplifies a suspension of cells in culture medium citing column 13 of Mickle. In addition, the applicant states that Mickle doesn't demonstrate a beneficial effect of collagen biograft implantation on cardiac developed pressure or left ventricular contractility, and that a subsequent publication by Mickle (Li et al.) shows that implantation of cell-seeded Gelfoam grafts does not improve ventricular function.

While applicant's arguments regarding the Li et al. reference were persuasive in regards to the methods of repairing a damaged myocardium, these arguments are not persuasive in overcoming the instant grounds of rejection over claims 16-18, and 22, which are product claims, and claims 19-21, and 24, which are method claims for making the product. In regards to the methods of making the product, the claims as written do not recite any particular use for the products made. In regards to the product claims, it is noted that the use of a product for a particular purpose is not afforded patentable weight in a product claim where the body of the

claim does not depend on the preamble for completeness but, instead, the structural limitations are able to stand alone. The MPEP states that,@.. in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art.@ In re Casey, 152 USPQ 235 (CCPA 1967); In re Otto , 136 USPQ 458, 459 (CCPA 1963)(MPEP 2111.02). Therefore, applicant's argument that neither Mickle et al. nor Shapiro et al. provide a reasonable expectation of success in improving ventricular function using the claimed biografts is not persuasive regarding the product and methods of making the product claims because in regards to these claims, the reasonable expectation of success is limited to whether the product can be made, not how it could be used.

Regarding the product and methods of making the product, the rejection of record as set forth in the previous office action states that Mickle et al. teaches a therapeutic graft comprising a biodegradable scaffold supporting cells comprising a combination of adult or pediatric cardiomyocytes and endothelial cells (Mickle et al., claims 9-19, and columns 5-6). Mickle et al. further teaches that the graft comprises growth factors including soluble angiogenic growth factors such as FGF or VEGF (Mickle et al., claims 17-18). In addition, Mickle et al. teaches that the cells for transplantation are autologous or allogeneic (Mickle et al, column 2).

Mickle et al. differs from the instant invention by teaching the use of biodegradable scaffolds made of collagen rather than alginate polysaccharides. Mickle et al. further differs by not specifically teaching that the soluble growth factors are contained in polymeric microspheres. Shapiro et al. supplements Mickle et al. by teaching the use of alginate polysaccharide as scaffolds for cells biografts (Shapiro et al., page 5). Specifically, Shapiro et al.

teaches methods of making a biodegradable graft where the cells are grown *in vitro* on or within the alginate polysaccharide matrix until they reach a desired state of differentiation (Shapiro et al., paragraph 2). Shapiro et al. further provides motivation for using the alginate polysaccharide matrix over other biodegradable matrixes, such as collagen, by teaching that collagen-based matrices have several disadvantages including the contraction of the collagen scaffold during in vitro culture which makes this scaffold unsuitable for prolonged in vitro cultivation of cells, and a rapid rate of degradation in vivo (Shapiro et al., page 3). Shapiro et al. states that because of the drawbacks of using collagen in matrixes, polysaccharide polymer scaffolds are preferred because they support the growth of thick layers of cells and are capable of maintaining the cells in an active functional state *in vitro* and *in vivo*, and are further amendable to vascularization (Shapiro et al., page 5). Shapiro et al. further supplements Mickle et al. by teaching that it is advantageous to include growth factors, particularly angiogenic growth factors, in the polysaccharide matrix in order to encourage more rapid growth of the cells on the matrix and to encourage vascularization, and that since growth factors are usually too small to be effectively retained within the polysaccharide matrix, they should be incorporated in the matrix in the form of controlled release microcapsules (Shapiro et al., page 11).

Therefore, in view of the substantial benefits to using alginate scaffolds over collagen scaffolds taught by Shapiro et al., it would have been *prima facie* obvious to the skilled artisan to substitute the alginate scaffolds containing controlled release microcapsules containing growth factors taught by Shapiro et al. for the collagen scaffolds containing soluble growth factors taught by Mickle et al. in the methods of making a cardiac biograft taught by Mickle et al. Further, based on the successful growth of cells in the alginate matrix taught by Shapiro et al.,

the skilled artisan would have had a reasonable expectation of success in making an alginate polysaccharide matrix containing autologous or allogeneic cardiomyocytes which further comprises controlled release polymeric microspheres capable of releasing soluble angiogenic factors.

Therefore, for the reasons discussed in detail above, the rejection of record is maintained over claims 16-21, 23, and 24.

Claims 1-3, 5-6, 9-10, and 22 are considered free of the prior art for reasons discussed in detail above and allowable at this time.

Specification

The objection to the abstract of the disclosure because it is in the form of a claim and contains legal phraseology is withdrawn in view of applicant's amendment of the abstract.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. The examiner can be reached Monday- Friday from 9:30-6:00 EST. If the examiner is not available, the examiner's supervisor, Ram Shukla, can be reached at (571) 272-0735. For all official communications, **the new technology center fax number is (571) 273-8300**. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER